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10/749,104	12/29/2003	Yuquan Wei	YX-2003-01US	3164

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,104	WEI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-98* is/are pending in the application.

4a) Of the above claim(s) *5,33,44-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-32 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Non-Final Rejection

Claims 1-98 are pending.

In view of the instant office action, the election/restriction mailed on 1/30/06 is vacated.

This application contains sequence disclosures that are encompassed by the definition for nucleotide sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements for Patent Applications Containing Nucleotide Sequence Disclosures.

Several pages (including pages 54-56, 58, 60, 61, 63, 66, 71, and 72) in the instant specification contain sequences that appear not to be listed in the CRF because they are missing a SEQ ID NO.

A complete response to the instant office action must include a response to the sequence compliance notification.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2-4, 6-16, 19-27, 32, 34-43, drawn to a vaccine comprising a DNA molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor, classifiable in class 514, subclass 44.

II. Claims 2, 3, 5-16, 19-25, 33-43, drawn to a vaccine comprising a protein molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor, classifiable in class 530, subclass 350.

III. Claim 44, drawn to a method of inhibiting in vitro growth of tumor cells expressing a tumor specific protein endogenously, classifiable in class 435, subclass 455.

IV. Claims 46-48, 50-61, 63-65, 67-76, drawn to a method of inhibiting growth of a tumor in a subject, the tumor expressing a tumor specific protein endogenously using a DNA molecule, classifiable in class 424, subclass 93.2.

V. Claims 46, 47, 49-61, 63, 64, 66-76, drawn to a method of inhibiting growth of a tumor in a subject expressing a tumor specific protein endogenously using a protein molecule, classifiable in class 514, subclass 2.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that the products would be used together. The DNA molecule (group I) and the protein (group IV) are unrelated as they utilize different products, which demonstrates that each product has a different mode of operation. Each invention performs this function using a structurally and divergent material. Therefore, each product is divergent in material. For these reasons the Inventions of I and II are patentably distinct.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the DNA molecule of group I can be used to inhibit growth of a tumor cell in vivo as opposed to its use in inhibiting growth of a tumor cell in vitro. Searching the inventions of groups I and III together would impose a serious search burden. The invention of Groups I and III have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the DNA molecule and the method of inhibiting growth of a tumor cell in vitro are not coextensive. Moreover, even if the DNA product were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

Invention II and III are unrelated because the product of group II is not used or otherwise involved in the process of group III.

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the DNA molecule of group I can be used to inhibit growth of a tumor cell in vitro as opposed to its use in inhibiting growth of a tumor cell in vivo. Searching the inventions of groups I and IV together would impose a serious search burden. The invention of Groups I and IV have a separate search status in the art as shown by their different

classifications. Moreover, in the instant case, the search for the DNA molecule and the method of inhibiting growth of a tumor cell in vivo are not coextensive. Moreover, even if the DNA product were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

Invention II and IV are unrelated because the product of group II is not used or otherwise involved in the process of group IV.

Invention I and V are unrelated because the product of group I is not used or otherwise involved in the process of group V.

Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein molecule of group II can be used to inhibit growth of a tumor cell in vivo as opposed to its use in inhibiting growth of a tumor cell in vitro. Searching the inventions of groups II and III together would impose a serious search burden. The invention of Groups II and III have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the protein molecule and the method of inhibiting growth of a tumor cell in vitro are not coextensive. Moreover, even if the protein product were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

Inventions II and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the

product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein molecule of group II can be used to inhibit growth of a tumor cell in vitro as opposed to its use in inhibiting growth of a tumor cell in vivo. Searching the inventions of groups II and V together would impose a serious search burden. The invention of Groups II and V have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the protein molecule and the method of inhibiting growth of a tumor cell in vivo are not coextensive. Moreover, even if the protein product were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

Claims 1, 17, 18, 25, 27, 28-31 link(s) inventions I and II. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 1, 17, 18, 25, 27, 28-31.

Claims 45, 62, and 77-86, link(s) inventions IV and V. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 45, 62, and 77-86.

Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional

application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re*

Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Because these inventions are distinct for the reasons given above and the search required for each Group listed above is not required for any other Group listed above and the search for each group is not co-extensive, restriction for examination purposes as indicated is proper.

It would be unduly burdensome for the examiner to search and consider patentability of all of the presently pending claims, a restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 § 1.17(h).

During a telephone conversation with Ben Wang on 5/31/06 a provisional election was made ~~without~~ with traverse to prosecute the invention of Group I, Claims 2-4, 6-16, 19-27, 32, 34-43. Affirmation of this election must be made by applicant in replying to this Office action. Claims and claims 5, 33, 44-86 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 87-98 are also withdrawn from the instant office action because the claims lack proper antecedent basis and the examiner cannot determine which claim the claims depend from because the claims recite "the vaccine of claim 77", however, claim 77 is directed to a method. If the claims are amended with proper antecedent basis with the response to the instant office action, than at that time the examiner will determine if another election/restriction is required or if the claims are embraced by a non-elected/elected invention.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in China on 12/27/02 and 12/25/03. It is noted, however, that applicant has not filed a certified copy of the Chinese applications as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless

the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings were received on 8/23/04. These drawings are not accepted.

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Figure 14 appears to a color photograph.

Specification

The disclosure is objected to because of the following informalities: The description for Figure 2 is missing description for 2F-1U.

Appropriate correction is required.

Claim Objections

Claim 17 is objected to because of the following informalities: the term "comprising" is misspelled on line 2. Appropriate correction is required.

Claim 27 is objected to because of the following informalities: is a missing a period at the end of the sentence. Appropriate correction is required.

Claims 13 and 41 are objected to because of the following informalities: an adenovirus is not modified by the peptide RGD. However, the fiber protein of an adenovirus is modified when the RGD motif is inserted into the fiber protein. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-32 and 34-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 6-8, 11-32, 34-36, and 39-43, as best understood, are readable on a genus of molecular homologs (DNA) to support the present claimed invention directed to a genus of DNA molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor such that the molecular homolog is capable of inducing an immune

response to the tumor specific protein in a subject bearing the tumor, wherein the genus of molecular homologs is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

Claims 9, 10, 37 and 38, as best understood, are readable on a genus of molecular homologs to support the present claimed invention directed to a genus of DNA molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor such that the molecular homolog is capable of inducing an immune response to the tumor specific protein in a subject bearing the tumor, wherein the tumor specific protein is an epidermal growth factor receptor having a structural similarity between the molecular homolog and EGFR ranges from 30% to 95%, wherein the genus of molecular homologs is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

The specification contemplates a genus of molecular homologs (DNA) to support the present claimed invention directed to a genus of DNA molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor such that the molecular homolog is capable of inducing an immune response to the tumor specific protein in a subject bearing the tumor (pages 4-5 and 12). The specification defines "molecular homolog" as a DNA molecular, which share similarity with another corresponding molecule (page 12). Thus, the definition is considered broad. The disclosure further contemplates a genus of molecular homologs having structural similarity to an epidermal growth factor receptor (EGFR), wherein the structure similarity between the molecular homolog and EGF ranges from 30-95%. The specification provides sufficient support for SEQ ID NOs for EGFR (page 26). However, since

the limitation "homolog having structural similarity to an epidermal growth factor receptor (EGFR), wherein the structure similarity between the molecular homolog and EGF ranges from 30-95%" is dependent on the claim reciting EGFR, EGFR is considered broader than EGFR. In addition, the specification does not provide sufficient description of a genus of molecular homologs and/or a genus of homologs having structural similarity to an epidermal growth factor receptor (EGFR), wherein the structure similarity between the molecular homolog and EGF ranges from 30-95%. There is a variation between the species embraced by the claimed genus. There is no structure-function correlation between EGFT and the claimed genus. The specification does not disclose how to make a representative number of species of the claimed genus with the desired biological function. The prior art does not supplement what is lacking in the specification for how to make a representative number of species of the claimed genus with the desired biological function. The skilled artisan would understand that not all molecular homologs embraced by the claimed genus cannot induce an immune response to the tumor specific protein in a subject bearing the tumor. It is not apparent that on the basis of the applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of molecular homologs that must exhibit the disclosed biological functions as contemplated by the specification.

It is not sufficient to contemplate a genus of molecular homologs (DNA) to support the present claimed invention directed to a genus of DNA molecule having sufficient structural similarity to a tumor specific protein endogenously expressed in a tumor such that the molecular

homolog is capable of inducing an immune response to the tumor specific protein in a subject bearing the tumor. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of a molecular homolog that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CAFC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CAFC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of molecular homolog having sufficient structural similarity to a tumor specific protein that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 43 recites the limitation "The method of claim 1" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 is not directed to a method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The limitation "the subject is an animal" in instant claims 14 and 42 does not have patentable weight over the prior art. See MPEP 2111.02.

The limitation "the subject is a human" in instant claims 15 and 43 does not have patentable weight over the prior art. See MPEP 2111.02.

The limitation "the tumor is selected from..." in instant claim 16 does not have patentable weight over the prior art. See MPEP 2111.02.

The limitation "the molecular homolog is generated using genetic engineering" in instant claim 3 does not have patentable weight over the prior art. See MPEP 211.02.

The specification defines "molecular homolog" as a DNA molecular, which shares similarity with another corresponding molecule (page 12). The term is very broad and can read on a nucleic acid encoding a protein e.g., a nucleic acid encoding the amino acid sequence comprising an EGFR with no modifications (e.g., amino acid substitutions/deletions) to the EGFR.

Claims 1-4, 6-12, 14-20, 22-25, 28-32, 34-40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Marciani (US 6,080,725). Marciani teaches a DNA vaccine comprising a nucleotide sequence encoding epidermal growth factor receptor (EGFR) (columns 9-10, 24-29, and 50-51). The construct can be formulated into a virus, including adenovirus (column 9). The construct can be with a pharmaceutically acceptable carrier (columns 50-51).

Claims 1-4, 6-12, 14-20, 22-25, 28-32, 34-40, and 42-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Uger et al. (US 20040002455). Uger teaches a composition comprising polynucleotide encoding an immunogen (pages 1-3 and 24). The immunogen can be EGFR (page 2). The composition can comprise an adenoviral vector or a lentiviral vector comprising the polynucleotide (pages 6-8). The skilled artisan understands that an adenovirus has a diameter 60-120 nm in diameter. The composition can comprise a nanoparticles comprising the polynucleotide (pages 6-9). The composition can further comprise a pharmaceutically acceptable carrier (page 25).

Claims 1-4, 8-10, 14-19, 25, 28-32, 36-38, and42-43 are rejected under 35 U.S.C. 102(a) as being anticipated by Lu et al. (The Journal of Immunology, 2003, 170:3162-3170). Lu teaches a DNA vaccine comprising a plasmid comprising a nucleic acid encoding EGFR (pages 3162-3163).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 11, 12, 13, 29, 39, 40, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uger et al. (US 20040002455) taken with Wickham et al. (US 5846782). Uger teaches a composition comprising polynucleotide encoding an immunogen (pages 1-3 and 24). The immunogen can be EGFR (page 2). The composition can comprise an adenoviral vector or a lentiviral vector comprising the polynucleotide (pages 6-8). One of ordinary skill in the art understands that an adenovirus has a diameter between 60-120 nm in diameter. The composition can comprise a nanoparticles comprising the polynucleotide (pages 6-9). However, Uger does not specifically teach using an adenovirus comprising a modified fiber protein.

However, at the time the invention was made, Wickham teaches an adenovirus comprising a fiber protein comprising a nonnative amino acid motif (RGD) (column 9). The adenovirus can be used to improve efficiency of deliver of a nucleic acid to a cancer cell (column 16). In view of the teaching of Wickham one of ordinary skill in the art would have a reasonable expectation of success to produce the adenovirus comprising a nucleic acid encoding EGFR.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Uger taken with Wickham, namely to make an adenovirus comprising a modified fiber protein containing an RGD motif. One of ordinary skill in the art would have been motivated to combine the teaching to increase the efficiency of delivering a nucleic acid to a cell using an adenovirus.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 19-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uger et al. (US 20040002455) taken with Levy et al. (US 6852704). Uger teaches a composition comprising polynucleotide encoding an immunogen (pages 1-3 and 24). The immunogen can be EGFR (page 2). The composition can comprise an adenoviral vector or a lentiviral vector comprising the polynucleotide (pages 6-8). One of ordinary skill in the art understands that an adenovirus has a diameter between 60-120 nm in diameter. The composition can comprise a nanoparticles comprising the polynucleotide (pages 6-9). However, Uger does not specifically teach using a nanoparticles having a diameter between 200nm-500nm.

However, at the time the invention was made, Levy teaches making and using a nanoparticles for delivering a nucleic acid to a cell wherein the nanoparticles preferably, the particle is a microparticle having a diameter preferably less than about 500 micrometers (columns 13 and 26-28). The nanoparticles comprises PLL, PLGA and a nucleic acid (columns 26-28). In view of the teaching of Levy one of ordinary skill in the art would have a reasonable expectation of success to produce a nanoparticle comprising a nucleic acid encoding EGFR.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Uger taken with Levy, namely to make a nanoparticles having a diameter between 200nm-500nm. One of ordinary skill in the art would have been motivated to combine the teaching to sufficiently deliver the nucleic acid to a cell as exemplified by Levy (columns 13 and 26-28).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Uger taken with Levy, namely to make a liposome or PLGA comprising the nucleic acid. One of ordinary skill in the art would have been motivated to combine the teaching to sufficiently deliver the nucleic acid to a cell as exemplified by Levy (columns 26-28).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uger et al. (US 20040002455) taken with Zauderer (US 6800442). Uger teaches a composition comprising polynucleotide encoding an immunogen (pages 1-3 and 24). The immunogen can be EGFR (page 2). The composition can comprise a vector comprising the polynucleotide (pages 6-8). However, Uger does not specifically teach a live vaccine comprising a genetically engineered bacterium comprising a nucleic acid encoding a tumor specific antigen.

However, at the time the invention was made, Zauderer teaches using a recombinant bacteria to express a tumor antigen (column 15-18). Zauderer teach that "live vaccine may be preferred because multiplication in the host leads to a prolonged stimulus of similar kind and magnitude to that occurring in natural infections, and therefore, confers substantial, long-lasting immunity (column 17, lines 62-66)." "Production of such live recombinant virus vaccine formulations may be accomplished using conventional methods involving propagation of the virus in cell culture or in the allantois of the chick embryo followed by purification (column 17, line 66-column 18, line)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Uger taken with Zauderer, namely to produce a live vaccine comprising a genetically engineered bacterium comprising a nucleic acid encoding a tumor specific protein. One of ordinary skill in the art would have been motivated to combine the teaching for producing a substantial, long-lasting immunity against the antigen.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Brian Whiteman

BRIAN WHITEMAN
PATENT EXAMINER

Notice to Comply	Application No. 10/749,104	Applicant(s) WEI et al.	
	Examiner B. Whiteman	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Several pages (including pages 60, 61, 63, 66, 71, 72) in the instant specification contain sequence that is not listed in the CRF.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification.**

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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